March 2, 2005

Sam Kennedy
Morflex, Inc.
2110 Highpoint Road
Greensboro, NC 27403

Dear Mr. Kennedy:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Acetyl tributyl citrate, posted on the ChemRTK HPV Challenge Program Web site on March 4, 2004. I commend Morflex, Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Morflex, Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/S/

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Acetyl Tributyl Citrate

Summary of EPA Comments

The sponsor, Morflex, Inc., submitted a test plan and robust summaries to EPA for acetyl tributyl citrate (CAS No. 77-90-7) dated December 29, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on March 4, 2004.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The submitter needs to resolve the discrepancy between the two submitted vapor pressure values or provide measured data.

2. Environmental Fate. The submitter needs to recalculate fugacity if the vapor pressure value is revised.

3. Health Effects. The submitted data for all endpoints are adequate for purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.

4. Ecological Effects. The submitted acute toxicity data for fish and aquatic invertebrates are adequate for the purposes of the HPV Challenge Program. The unsupported estimated algal toxicity data are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured data on the sponsored chemical.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Acetyl Tributyl Citrate Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data provided by the submitter for melting point, boiling point, partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program.

Vapor Pressure. The submitted vapor pressure value of 0.052 mm Hg at 20 °C for acetyl tributyl citrate (99.0%) was obtained from a company report (Morflex 1998); no experimental details are available in the summary. The submitter also provided an estimated value of 0.000485 mm Hg at 25 °C using MPBPWIN v1.40. These values differ by a factor of 100. The submitter needs to check the accuracy of the vapor pressure value of 0.052 mm Hg at 20 °C, and clearly indicate whether this is a measured or estimated value; if measured, the method used needs to be stated. If this information is not available then the submitter needs to provide measured vapor pressure data following OECD TG 104 (estimated vapor pressure values above 7.5×10^{-8} mm Hg (1×10^{-5} Pa) are not adequate for the purposes of the HPV Challenge Program).

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation, stability in water, and biodegradation are adequate for the purposes of the HPV Challenge Program.

Fugacity. The submitter obtained fugacity values using the Level III Fugacity Model in EPIWIN v3.10 with a vapor pressure input of 0.052 mm Hg. However, the distributions in air, water, soil and sediment differ significantly when the estimated vapor pressure of 4.85×10^{-4} mm Hg is used in this model. If a revised measured vapor pressure value is obtained (see previous section) a recalculation of fugacity is needed .

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitted data for all endpoints are adequate for purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.

Ecological Effects (fish, invertebrates, and algae)

The submitted data for fish (7-day larval survival test in fathead minnow) and aquatic invertebrates are adequate for the purposes of the HPV Challenge Program.

Algae. An ECOSAR-estimated EC_{50} value, in the absence of adequate measured analog data, does not address the endpoint for the purposes of the HPV Challenge Program. Moreover, the ECOSAR model is not a good predictive tool for compounds such as this one with multiple ester groups. The submitter needs to provide measured data on the sponsored chemical.

Specific Comments on the Robust Summaries

General

The submitter needs to designate each key study in the "Remarks" section of its robust summary.

Health Effects

Genetic Toxicity (gene mutations). The key study (Gollapudi and Linscombe, 1988) summary lacked the following information: individual cell counts at each concentration, criteria for a positive response, and whether controls showed appropriate responses. The summary of the unscheduled DNA synthesis assay was missing information on the guideline followed, GLP status, test substance purity, statistical methods used, and cytotoxicity. The remarks section (p 82) of the mammalian cell forward mutation assay is confusing. The data should be tabulated to make it easier to understand.

Reproductive Toxicity. The summary of the GLP-compliant 2-generation reproductive toxicity feeding study was missing a list of reproductive organs examined (although retention of a full range of tissues was reported).

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.